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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,708	09/18/2003	Steven T. Brentano	GP107-03.DV1	6892

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EXAMINER	
SWITZER, JULIET CAROLINE	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,708	BRENTANO ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group II, claims 13-20 in the reply filed on 5/5/06 is acknowledged. The traversal is on the ground(s) that it would not pose an undue burden on the examiner to search and examiner the claims together. This is not found persuasive because it would pose as serious burden on the examiner to search and examine both inventions because, a search for the inventions of the two groups would not be coextensive because a search indicating the process is novel or unobvious would not extend to a holding that the products themselves are novel or unobvious; similarly, a search indicating that the product is known or would have been obvious would not extent to a holding that the process is known or would have been obvious. Therefore, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

2. Applicant's request for rejoinder is acknowledged, and applicant is reminded of their duty to maintain pending method claims to be commensurate in scope with product claims in order to preserve their right to rejoinder.

3. Regarding claims 14 and 20, these claims require that the "at least one second oligonucleotide" be a sequence "having" SEQ ID NO: 24. Neither of these claims sets forth that the second oligonucleotide "consist" of SEQ ID NO: 24, and so the claims do not conflict with the requirements of independent claim 13. However, it is noted that instant a primer consisting of SEQ ID NO: 24 does not qualify to be a second oligonucleotide within the limitations of claim

13 since SEQ ID NO: 24 does not have three to seven bases 5' to the eighteen contiguous bases contained in SEQ ID NO: 24.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 13, 14, 15, 19, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13, 14, 15, 19, and 20 are indefinite because the requirements regarding the second oligonucleotide appear to be internally inconsistent and are therefore confusing. Namely, the second oligonucleotide "is an oligonucleotide consisting of 19 to 25 bases" implies that a molecule of as few as 19 nucleotides can meet the limitations of this phrase, but the next limitation requires that the molecule contain 18 contiguous bases contained in SEQ ID NO: 24 plus 3 to 7 additional bases 5' to the 18 contiguous bases. Thus, the second part requires that the second oligonucleotide be at least 21 nucleotides long, which conflicts with the first limitation. Clarification is required.

Claim Rejections - 35 USC § 102

6. Claims 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank X53896, GI: 44201, published 04 September 1991.

For these claims the word "kit" is being broadly interpreted so as to include the teaching of the recited reagents or molecules since a "kit." The word "kit" does not provide any structural requirement, and is being treated as a recitation of intended use. The GenBank record teaches

an nucleic acid molecule comprising partial 16S rRNA sequence from *Mycobacterium cookii*.. . Regarding claim 16, the record teaches an oligonucleotide having each of SEQ ID NO: 21-24. Namely, SEQ ID NO: 21 is identical to nucleotides 58-82, SEQ ID NO: 22 is identical to nucleotides 59-82, SEQ ID NO: 23 is identical to nucleotides 62-83, and SEQ ID NO: 24 is identical to nucleotides 65-83 of the sequence given in the GenBank record. Thus the record teaches the molecule claimed in claim 16.

Regarding claim 17, this claim is broadly drawn to require any oligonucleotide "of SEQ ID NO: 11." An oligonucleotide "of SEQ ID NO: 11" is interpreted to require as few as two nucleotides of SEQ ID NO: 11. The sequence taught in the GenBank record contains many fragments of SEQ ID NO: 11, each of which are oligonucleotides "of" SEQ ID NO: 11.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kazda et al. (International Journal of Systemic Bacteriology, July 1990, p. 217-223) in view of GenBank X53896, GI: 44201, published 04 September 1991.

For these claims the word "kit" is being broadly interpreted so as to include the teaching of the recited reagents or molecules since a "kit." The word "kit" does not provide any structural requirement, and is being treated as a recitation of intended use.

Kazda et al. teach isolated nucleic acid molecules that are the product of long range reverse transcript generated stretches of 16S rRNA of M. cookii (p. 217, 2nd column). Kazda et al. give the partial sequence of 16S rRNA in figure 1. The reverse transcript procedure would have resulted in multiple copies of double stranded molecules, that is the strand recited in the figure would have been present hybridized to a complementary strand. Thus, the reaction product would have had multiple first and second oligonucleotide molecules.

Kazda et al. to not teach a molecule having a sequence selected from the group of sequences SEQ ID NO: 21-24.

The GenBank record teaches an nucleic acid molecule comprising partial 16S rRNA sequence from *Mycobacterium cookii*. Regarding claim 16, the record teaches an oligonucleotide having each of SEQ ID NO: 21-24. Namely, SEQ ID NO: 21 is identical to nucleotides 58-82, SEQ ID NO: 22 is identical to nucleotides 59-82, SEQ ID NO: 23 is identical to nucleotides 62-83, and SEQ ID NO: 24 is identical to nucleotides 65-83 of the sequence given in the GenBank record. Thus the record teaches the molecule claimed in claim 16.

Regarding claim 17, this claim is broadly drawn to require any oligonucleotide "of SEQ ID NO: 11." An oligonucleotide "of SEQ ID NO: 11" is interpreted to require as few as two

nucleotides of SEQ ID NO: 11. The sequence taught in the GenBank record contains many fragments of SEQ ID NO: 11, each of which are oligonucleotides "of" SEQ ID NO: 11. The sequence taught in the GenBank record also comprises the complement of instant SEQ ID NO: 11 at nucleotides 341-367.

The sequences set forth in claim 18 have been addressed. As with claim 17, it is noted that in these claims the requirement that the claimed oligonucleotides have sequences "of" the recited SEQ ID NO is extremely broad, requiring that the claimed compositions have only small portions of the recited sequences.

It would have been prima facie obvious to have modified the methods taught by Kazda et al. so as to have amplified additional 5' portions of the M. cookii sequence that were taught by Kazda et al. Such amplification products would have included the compositions set forth in the claimed methods, since the amplification products would have been double stranded they would have comprised all of the recited SEQ ID NO, and there inherently would have been multiple copies following a reverse transcription reaction, which would have provided multiple first and second oligonucleotides. One would have been motivated to undertake such amplification in order to provide copies of the gene encoding the 16S rRNA for future analysis of the newly discovered species of Mycobacteria.

10. Claims 13-15 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hogan et al. (US 5677128) in view of GenBank X53896, GI: 44201, published 04 September 1991, and further in view of McAllister et al. (US 5908744).

Hogan et al. teach compositions comprising oligonucleotide probes that target the 16S rRNA region of Mycobacterium species (Col. 2, lines 40-45, for example). Hogan et al. teach

that oligonucleotide probes preferred in their invention are between about 15 and 50 bases (Col. 10, lines 10-14). Hogan et al. teach examples wherein an oligonucleotide specific for a single species of Mycobacterium was identified (Example 1), and wherein an oligonucleotide specific for the genus Mycobacterium was identified (Example 3). In each case, the oligonucleotide were identified based on examination of an of various 16s rRNA sequences (see Examples). Furthermore, Hogan et al. provide specific guidance for the selection of oligonucleotides, teaching, for example,

> "Once the variable regions are identified, the sequences are aligned to reveal areas of maximum homology or 'match'. At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
>
> First, probes should be positioned so as to minimize the stability of the probe:nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe:target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G:C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10°C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structures inhibitory to hybridization are less preferred. Finally, probes with extensive self complementarity should be avoided (Col. 6, line 48-Col. 7, line 13)."

Hogan et al. teach that the oligonucleotides can be packaged into kits (Col. 66, line 14).

Hogan et al. do not teach oligonucleotides that comprise an oligonucleotide in a size range of about 19 to 25 bases containing 18 contiguous bases of SEQ ID NO: 24, or any of the additional nucleic acids required in the instant claims.

The GenBank record teaches an nucleic acid molecule comprising partial 16S rRNA sequence from *Mycobacterium cookii*. Regarding claim 16, the record teaches an oligonucleotide having each of SEQ ID NO: 21-24. Namely, SEQ ID NO: 21 is identical to nucleotides 58-82, SEQ ID NO: 22 is identical to nucleotides 59-82, SEQ ID NO: 23 is identical to nucleotides 62-83, and SEQ ID NO: 24 is identical to nucleotides 65-83 of the sequence given in the GenBank record. Additionally the record provides nucleotides 5' to the portion which comprises SEQ ID NO: 24.

Regarding claim 14, this claim is broadly drawn to require any oligonucleotide "of SEQ ID NO: 11." An oligonucleotide "of SEQ ID NO: 11" is interpreted to require as few as two nucleotides of SEQ ID NO: 11. The sequence taught in the GenBank record contains many fragments of SEQ ID NO: 11, each of which are oligonucleotides "of" SEQ ID NO: 11. The sequence taught in the GenBank record also comprises the complement of instant SEQ ID NO: 11 at nucleotides 341-367.

The sequences set forth in claims 15, 19, and 20 have been addressed. It is noted that in these claims the requirement that the claimed oligonucleotides have sequences "of" the recited SEQ ID NO is extremely broad, requiring that the claimed compositions have only small portions of the recited sequences.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have selected oligonucleotides from within the GenBank sequence useful for the amplification of M. cookii sequences. The selection of any oligonucleotide from within this sequence would have been expected to function equivalently with regard to the ability to M. cookii 16S sequences. One would have been motivated to provide primers that comprised any

of the fragments of the GenBank record in order to provide a means for the amplification and detection of this Mycobacteria species.

These do not provide a composition wherein the first oligonucleotide primer is modified to include a 5' promoter sequence. However, compositions for amplifying nucleic acids wherein one of the primers is modified to include a 5' promoter sequence were routine in the prior art at the time the invention was made. For example, McAllister et al. teach compositions and kits for synthesizing multiple copies of target nucleic acid which use a promoter-primer to initiate DNA and RNA synthesis, and that such methods preferably reduce non-specific product formation (See Abstract, for example, and Col. 4). McAllister et al. teach that preferred promoters include the T7 bacteriophage promoter (Col. 11, lines 5-10). McAllister et al. exemplify the use of such primers for the detection of Mycobacterium (Col. 13-15).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the compositions taught by Hogan et al. in view of the GenBank record to have included a primer that is modified to include a 5' promoter sequence, particularly a T7 promoter sequence. The ordinary practitioner would have been motivated to make such compositions in order to carry out methods such as those taught by McAllister et al. and thereby to exploit the advantages of such methods, since McAllister et al. specifically teach that such methods reduce side reactions, and improve amplification (Col. 10, lines 39-58).

11. Claims 13-15 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over McAllister et al. (US 5908744). in view of GenBank X53896, GI: 44201, published 04

September 1991, and further in view of Buck et al. (BioTechniques, 27:528-536, September 1999).

McAllister et al. teach compositions and kits for synthesizing multiple copies of target nucleic acid which use a promoter-primer to initiate DNA and RNA synthesis, and that such methods preferably reduce non-specific product formation (See Abstract, for example, and Col. 4). McAllister et al. teach that preferred promoters include the T7 bacteriophage promoter (Col. 11, lines 5-10). McAllister et al. exemplify the use of such primers for the detection of Mycobacterium (Col. 13-15).

McAllister et al. do not teach oligonucleotides that comprise an oligonucleotide in a size range of about 19 to 25 bases containing 18 contiguous bases of SEQ ID NO: 24, or any of the additional nucleic acids required in the instant claims.

The GenBank record teaches an nucleic acid molecule comprising partial 16S rRNA sequence from *Mycobacterium cookii*. Regarding claim 16, the record teaches an oligonucleotide having each of SEQ ID NO: 21-24. Namely, SEQ ID NO: 21 is identical to nucleotides 58-82, SEQ ID NO: 22 is identical to nucleotides 59-82, SEQ ID NO: 23 is identical to nucleotides 62-83, and SEQ ID NO: 24 is identical to nucleotides 65-83 of the sequence given in the GenBank record. Additionally the record provides nucleotides 5' to the portion which comprises SEQ ID NO: 24.

Regarding claim 14, this claim is broadly drawn to require any oligonucleotide "of SEQ ID NO: 11." An oligonucleotide "of SEQ ID NO: 11" is interpreted to require as few as two nucleotides of SEQ ID NO: 11. The sequence taught in the GenBank record contains many fragments of SEQ ID NO: 11, each of which are oligonucleotides "of" SEQ ID NO: 11. The

sequence taught in the GenBank record also comprises the complement of instant SEQ ID NO: 11 at nucleotides 341-367.

The sequences set forth in claims 15, 19, and 20 have been addressed. It is noted that in these claims the requirement that the claimed oligonucleotides have sequences "of" the recited SEQ ID NO is extremely broad, requiring that the claimed compositions have only small portions of the recited sequences.

Further, Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Thus, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have selected oligonucleotides from within the GenBank sequence useful for the amplification of M. cookii sequences. The selection of any oligonucleotide from within this sequence would have been expected to function equivalently with regard to the ability to M. cookii 16S sequences. One would have been motivated to provide primers that comprised any of the fragments of the GenBank record in order to provide a means for the amplification and detection of this Mycobacteria species. Further, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified any of the primers selected to have included a primer that is modified to include a 5' promoter sequence, particularly a T7 promoter sequence. The ordinary practitioner would have been motivated to make such compositions in order to carry out methods such as those taught by McAllister et al. and thereby to exploit the advantages of such methods, since McAllister et al. specifically teach that such methods reduce side reactions, and improve amplification (Col. 10, lines 39-58).

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

July 20, 2006